PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference PB60024	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2004/001016	International filing date *(day/month/year)* 02 February 2004 (02.02.2004)	Priority date *(day/month/year)* 19 March 2003 (19.03.2003)]
International Patent Classification (IPC) or national classification and IPC [7] A61K 39/395, A61P 25/00 // C07K 16:28		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 23 September 2005 (23.09.2005)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Ellen Moyse
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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23 SEP 2004
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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/001016	02.02.2004	19.03.2003

International Patent Classification (IPC) or both national classification and IPC
A61K39/395, A61P25/00

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,3-19

because:

☒ the said international application, or the said claims Nos. 1,3-19 (method of treatment) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9-18
	No:	Claims	1-8,19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-19
Industrial applicability (IA)	Yes:	Claims	2
	No:	Claims	1,3-19

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1 and 3-19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 02/062383 A (VINSON MARY ;IRVING ELAINE ALISON (GB); SMITHKLINE BEECHAM PLC (GB) 15 August 2002

D2: WO 95/22344 A (BRAUN PETER ERICH ;MCKERRACHER LISA JOAN (CA); UNIV MCGILL (CA); D) 24 August 1995

1 NOVELTY

1.1 D1 discloses altered anti-MAG antibodies characterized by the amino acid sequences of the CDRs and their use for treating stroke and neurological diseases. CDRs of the light and heavy chains have high homology with those of claim 6 (claims 1-16). The feature of promoting oligodendrocyte survival does not limit the scope of claim 1 and is therefore not taken into account (see the clarity section below) for assessing claims 1-5 which are not novel over the disclosure of D1. The CDR1 of the light chain and the CDR3 of the heavy chain as disclosed in D1 are the same as the ones of claim 6. Since in claims 6-8 the altered antibody is defined by only one CDR (claim 6), by one CDR of the light chain and one of the heavy chain (claim 7) or by generic terms (claim 8), claims 6-8 & 19 are not novel over D1.

1.2 Claims 9-18 are novel over the disclosure of D1 since they relate to an antibody defined by at least the three CDRs of the light chain or the three CDR of the heavy

2.4 The same reasoning applies for claim 10 which is related to the use of an antibody not completely defined. Claims 11-18, related to the use of well-defined antibodies made of a light chain AND a heavy chain are not considered as involving an inventive step for the reason mentioned above on the point 2.3.

3 INDUSTRIAL APPLICABILITY

3.1 For the assessment of the present claims 1 and 3-19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII

1 CLARITY & SUPPORT

1.1 The terms "altered", "or a functional fragment thereof" and *fragment thereof" used throughout the claims are vague and unclear and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of the claims unclear (Article 6 PCT). The use of the term "functional fragment thereof" when no function is disclosed in the claim is not clear.

1.2 The subject-matter of claim 6-10 is not clearly defined since characterizing an antibody only by one CDR (claim 6), by one CDR of the light chain and one of the heavy chain (claim 7), by the three CDRs of the light chain or of the heavy chain (claim 8) or by the light chain or the heavy chain (claims 9 & 10) is not sufficient to define an antibody.

chain or by sequences that are novel.

1.3 Document D2 discloses the use of MAG antagonists such as chimeric human/mouse anti-MAG antibodies for treating strokes and other neurological diseases (p.16, l.21 - p.19, l.14). The claims 1-5 are therefore not novel over D2.

2 INVENTIVE STEP

2.1 Claims 9-18 are novel but do not involve an inventive step for the following reason. Document D1 which is considered to represent the most relevant state of the art, discloses the use of altered anti-MAG antibodies characterized by the amino acid sequences of the CDRs for treating stroke and neurological diseases. CDRs of the light and heavy chains have high homology with those of claim 6 (claims 1-16). The subject-matter of claim 9 differs in that it refers to the use of an anti-MAG antibody or functional fragment thereof comprises a heavy chain of sequences ID NO 7 or 9 and/or light chain sequence ID NO 8. The problem to be solved by the present invention may therefore be regarded as the use of an alternative anti-MAG antibody for treating stroke and neurological diseases.

2.2 Firstly it is considered that the proposed solution is not solving the problem over the whole scope of the claim since an antibody is defined by a licht chain AND an heavy chain. Therefore only the part of the claim related to a completely defined antibody is considered to solve the problem posed. The part of the claim related to an heavy chain or a light chain is not solving the problem, and the claim is not considered as involving an inventive step.

2.3 Secondly the use of an alternative well-defined anti-MAG antibody is also not considered as involving an inventive step since it is a matter of routine to prepare alternative humanized antibodies. Although the antibodies characterized by the sequences ID 7 or 9 AND 8 are new, their use for treating neurological diseases is not considered as involving an inventive step since such use is disclosed in D1. The antibodies are simply used according to their predicable functioning. Consequently the subject-matter of claim 9 is not considered to involve an inventive step (Article 33(3) PCT).